Diabetic Neuropathy Pain Management ("DNPM")

Diabetic neuropathy is one of the most common forms of peripheral neuropathy, a type of nerve damage that can occur in diabetes (Type 1 or 2). High blood glucose levels due to diabetes can damage nerve fibers throughout body, but diabetic neuropathy mostly often damages nerves in the hands and feet. It causes symptoms such as tingling, numbness, burning and pain. These symptoms are mild for some people but they can be painful, disabling and even fatal for others. The pathology of diabetic neuropathy is still unknown and there is no treatment to cure diabetic neuropathy. Current treatment is to reduce the pain associated with diabetic neuropathy (symptomatic treatment). According to a report from Data Bridge Market Research, there was an approximately $3.9 billion worldwide market in 2022 for treating diabetic neuropathy pain.

The symptomatic treatment typically involves the use of antidepressants, anticonvulsants or opioid or opioid-like medications taken orally. Concerns related to potential side effects with these oral medications prevent their use with many patients. Most of these drugs work through systemic effects mainly on the spinal cord and/or the brain (i.e. central nervous system) to reduce the pain caused by diabetic neuropathy. However, antidepressants and anticonvulsants taken orally possess significant systemic side effects such as insomnia, dizziness, dry mouth, weight gain, headache and nausea. The long-term use of opioids or opioid-like medications may cause serious addiction. So far, there are only three oral medications approved by the FDA for treating diabetic neuropathy; duloxetine ("Cymbalta", anti-depressant), pregabalin ("Lyrica", anti-convulsant) and tapentadol ("Nucynta", opioid). They are known to be suboptimal in reducing pains with only about 50% effectiveness for diabetic neuropathy patients.

Numerous mechanisms related to transduction or transmission functions have been linked in causing diabetic neuropathy pain. These transduction or transmission functions involve multiple receptors. Typically, the above oral medications for treating painful diabetic neuropathy act at one specific receptor site. Each patient may have different mechanism(s) as the cause their pain. This may explain why, for example, antidepressants show a good efficacy for some patients but not for other patients. Since it is difficult to predict for any given patient the target and correct receptor site, the outcome of prescribed medications is unpredictable. Using multiple oral medications for targeting various receptor sites is not a viable option due to their cumulative side effects and adverse drug-drug interactions.

Our Approach

Postsurgical Therapeutics, Inc. ("PTI") is developing a controlled, sustained delivery of pain medications via encapsulation in biodegradable polymers such as PLGA ("DNPM product"). Our DNPM product using local delivery of pain management medications may reduce the pain caused by diabetic neuropathy without the systemic side effects associated with medications delivered orally. In addition, multiple medications can be administered locally to target multiple receptors without causing systemic side effects and adverse drug-drug interactions. Since the plasma

concentration of locally delivered medications is only 5 to 10 percent of the corresponding oral medications, the incidence of systemic side effects and adverse drug-drug interactions is dramatically reduced compared to the systemic use of the same medications delivered orally.

Our DNPM product provides a method for treating diabetic neuropathy and consists of comprehensive set of pain management medications such as sodium channel blockers, α-2 adrenergic receptor agonists and anti-inflammatory drugs. These medications can be encapsulated in PLGA microspheres for controlled, sustained release over 2 – 8 weeks. These medications can be administered by a commercial painless micro-needle patch or injection device. This user-friendly injection method enables the injecting of a small amount of pain management medications at multiple sites which can enhance the efficacy of treatment.

Product Development

PTI sold its IP rights to Upex-Med in February, 2019 through transfer by Kossen. PTI and Upex-Med are co-developing this product. We completed developing 5 pain medication-PLGA microsphere formulations and performed their efficacy animal testing. This animal testing used two animal models, von Frey filament test and thermal hyperalgesia paw withdrawal latency response test, after chronic constriction injury to create the pain associated with diabetic neuropathy. We used 14-day drug release formulations to screen the efficacy of each drug as well as their combination. We found that the combination of PLGA microspheres of carbamazepine (anti-epileptic drug), celecoxib (COX-2 inhibitor) and lidocaine (local analgesia) showed the best efficacy.

Regulatory Approval in the U.S.

PTI believes the product will be eligible for the FDA's 505(b)(2) NDA approval path in the U.S. ("repurposed drug") rather than the 505(b)(1) NDA approval path required for new drugs. The 505(b)(2) NDA approval path allows the developer of a new formulation of an approved therapeutic agent to reference the safety and efficacy data on which the therapeutic agent was approved. Depending on clinical requirements, product development and approval by the 505(b)(2) NDA approval can take less than five – six years from the date of IND approval.

Intellectual Property

We obtained the issuance of the US patent on February 7, 2023 (US #11,571,429).

Commercialization Strategy

Upon completing the efficacy animal testing, we will seek for a corporate partnership to complete development, obtain regulatory approvals and commercialize worldwide. We expect the partnership to provide near term cash, including an upfront license fee, and milestone payments.